REMARKS

Claims 8-27 are pending. Claims 8-15 and 30 are withdrawn. Claims 16-19 and 21-27 are under consideration.

Applicants submit a paper copy of the sequence listing and an accompanying statement pursuant to 37 CFR § 1. 821(c) and (g) as requested by the Examiner. This Response accompanies a Request for Continued Examination. Applicants request consideration of the Information Disclosure Statement submitted May 22, 2009.

Rejections under 35 USC 102(b)

Claims 16-19, 21, 27 are rejected as anticipated by Wang et al., JBC 271:23811-17, 2006 ("Wang"), as evidenced by Gulbis et al., Cell 97:943-52, 1999 ("Gulbis"). The rejection is traversed.

Claim 16 requires the presence of a surface to which is attached a cytosolic accessory protein (emphasis added). Attachment to a surface is described in the application at various points. For example, page 3 refers to "an array based method whereby the in vitro binding of soluble functional domains of membrane bound proteins, such as ion channels, cell surface receptors and transporters to arrays of immobilized cytoplasmic accessory proteins can be characterized in detail. Page 9 of the specification also notes that "arrays according to the invention can comprise tagged protein constructs that are each expressed and immobilized in a functional manner in a spatially defined format". The nature of attachment to a surface is further described on page 11 lines 14-20, which refer to non-specific attachment to a surface for example by physical absorption or by formation of covalent interactions, or by attachment through a common marker moiety linked to each protein.

Wang fails to suggest this feature of the claimed invention. This reference describes the use of a yeast two hybrid system to study the interaction of Kv α and β subunits. Applicants note the Examiner's assertion that "[s]aid voltage gated potassium channel β 1.3

subunits which do not interact with said α subunit provide a surface having attached thereto at least one cytosolic accessory protein of a membrane protein selected from ion channels wherein said cytosolic accessory protein is free from membrane protein components or other subunits of said ion channel as set forth in claim 16." The Examiner appears to be stating that Wang provides a surface to which is attached a β 1.3 subunit that is not interacting with any other membrane protein components or subunits of the ion channel.

What is not apparent, however, is the surface to which the Examiner refers. If one assumes that the surface is to be taken as the cell membrane, there is no evidence that the subunit when expressed in the absence of its subunit binding partner is attached to the cell membrane. The yeast two hybrid system typically uses β galactosidase activation domains or binding domains expressed as fusion proteins with the two potential interacting protein partners. Where the two protein partners do interact the β galactosidase activation and binding domains are brought together and are able to bring about the expression of β galactosidase, which can be detected in the yeast system. Generally, the yeast two hybrid system includes nuclear localization signals for the β galactosidase activation and binding domain parts of the fusion protein such that the expressed proteins are targeted to the yeast nucleus. This is necessary in order to bring the activation and binding domains together in a region of the cell where they will have the opportunity to bind to the relevant promoter regions of the β galactosidase gene and effect expression of β galactosidase. Therefore, even in the absence of expression of the Kvα subunit binding partner of the expressed β subunit the lone β subunit will not associate with the membrane, and so cannot be considered as being attached to a surface.

Furthermore, even if the β 1.3 subunit is expressed in a cell in the absence of the α subunit, or in the absence of other localization signals such as the nuclear localization signal used in the yeast two hybrid system, there is nothing that would indicate that the β subunit alone is associated with the membrane, let alone attached to the membrane. Gulbis states at page 943, column 1, that "[m]any voltage dependent K+ channels have a non integral membrane component known as the β subunit ... Four α subunits form the transmembrane channel for K+ ion conduction and voltage-dependent gating, while the β subunit is attached to the cytoplasmic face of the α subunits." Thus, the α subunits are the subunits which can be taken to be attached to the

membrane, with the β subunits interacting specifically with the α subunits and not with the membrane itself. No structural features of the β subunit are described in Gulbis that would lead the β subunits to interact with the membrane directly, that is, in the absence of any other subunits. Therefore expression of the β subunit alone, in the absence of its binding a subunit would not result in a β subunit attached to the membrane.

The foregoing assumes that the Examiner intends the surface of claim 16 to be understood as referring to the membrane of the yeast cells described in Wang. Another possible interpretation could be that the surface that is referred to is taken as being equivalent to the yeast cell culture plates pictured in Figure 3, with the growth of yeast on those plates being somehow equivalent to attachment of the β subunit to a surface. Even under this interpretation, however, Wang cannot be said to teach the requirement of claim 16 of a surface to which is attached a cytosolic accessory protein.

First, the yeast cells are not attached to the plate surface; they are merely grown on media disposed therein. Second, the β 1.3 subunits are being expressed in a living cell system, which inherently involves the simultaneous expression of a multitude of membrane protein components belonging to the yeast cell. The plating of yeast cells in a culture plate cannot therefore be considered equivalent to the attachment of a β 1.3 subunit to a surface to form an array. Indeed, even if the yeast cells were considered to be attached to the plate surface, the β subunit cannot be considered to be attached to the yeast cells in any meaningful way, since the β1.3 subunits are expressed cytoplasmically within the yeast cells. Therefore, even under the latter interpretation this arrangement does not read on claim 16.

Wang therefore fails to describe the features of claim 16 and does not anticipate the claimed invention. For the same reasons, Wang fails to describe the remaining claims subject to the rejection, as claims 17-19, 21, and 27 depend from claim 16. Applicants request reconsideration and withdrawal of the rejection for anticipation.

Rejections under 35 USC § 103(a)

Claims 16-19 and 21-27 are rejected as unpatentable over Wang as evidenced by Gulbis in view of Charych et al. II, US Patent No. 7,148,058 ("Charych"). The rejection is traversed.

As set forth above, Wang, as evidenced by Gulbis does not describe a cytosolic accessory protein attached to a surface. The Examiner suggests that it nevertheless would have been obvious for one of skill in the art "to analyze the Kv channel 13 beta 1.3 subunits of Wang by anchoring to the protein microarrays on mirrored substrates in the manner of Charych." Applicants disagree.

Charych describes the anchoring of isolated proteins onto a surface (for example, the Abstract states that "the protein array elements may be attached directly to an organic functionalized mirrored substrate by binding reaction between functional groups on the substrate (e.g. amine) and protein (e.g. activated carboxylic acid).")

Wang does not teach isolated protein subunits, but simply teaches expression of the β subunit in the yeast two hybrid system, or in Xenopus oocytes. Wang does not describe the isolation of any of these β subunits. Still less does Wang disclose any way in which the subunits may be isolated. The skilled person would not be motivated to consider combining the teachings of Wang with those of Charych, since Wang does not provide protein array elements in a form suitable for use with the microarrays of Charych. Charych does not provide any teaching for attaching membrane bound proteins or cytosolic proteins expressed in whole cells to a surface for use as a protein microarray. Therefore, Wang and Charych cannot be combined to produce the claimed invention.

Applicants request reconsideration and withdrawal of the rejection for obviousness.

Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A request for continued examination accompanies this response. Please charge any

additional fees due, or credit any overpayment of same, to Deposit Account Number: 50-0311, Customer Number: 35437, Reference Number: 33694508001US.

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